

L93 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2003 ACS

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DOCUMENT NUMBER: 128:98545
TITLE: **Inhibitors of alternative alleles**
of genes as a basis for cancer therapeutic agents
INVENTOR(S): **Housman, David E.**
PATENT ASSIGNEE(S): K.O. Technology, Inc., USA
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US 5702890	A	19971230	US 1995-379680	19950404
WO 9503335	A1	19950202	WO 1994-US8473	19940726
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US 6054273	A	20000425	US 1997-967454	19971111
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AB This invention is directed to a therapeutic strategy, involving (1) identification of alternative **alleles** of genes coding for proteins vital for cell viability or cell growth and the loss of one of these **alleles** in cancer cells due to loss of heterozygosity (LOH) and (2) the development of **inhibitors** with high specificity for the single remaining alternative **allele** of the vital gene retained by the cancer cell after LOH. The **inhibitors** of this invention are **specific** for one alternative **allele** of a gene that codes for a protein vital to cell viability or cell growth. The targeted gene has two alternative **alleles** in which the **inhibitors** of this invention block only the one alternative **allele** still present in the cancer cells. Exposure to the **inhibitor** **inhibits** or kills cancer cells which have undergone LOH. Protein is still capable of being expressed in the normal cells exposed to the **inhibitor** by the unblocked alternative **allele**. This differential effect of the **inhibitor** on cancer cells and normal cells accounts for the high therapeutic index of the **inhibitors** of this invention when used as antineoplastic agents. The method is exemplified by treatment of human solid tumors with **allele-specific antibodies** against the human transferrin receptor. The method also can be used in targeted drug design, such as with dihydrofolate reductase **allele-specific inhibitors**. Examples of **allele-specific inhibitors** include **ribozymes**, **oligopeptides**, **oligonucleotides**, **antibody** or **antibody fragments**, and low-mol.-wt proteins.

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INVENTOR(S): **Housman, David E.**
PATENT ASSIGNEE(S): K.O. Technology, Inc., USA
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